

### **REMARKS/ARGUMENTS**

Claims 33 and 35-45 remain under examination in this application. Claims 33 and 41 have been amended as discussed below. The amendments to claim 33 find support in the specification on page 16, first complete paragraph. No new matter has been added as a result of the claim amendments.

By the amendments, Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

#### **35 U.S.C. §112 Rejections**

Claims 41 has been rejected under 35 U.S.C. §112, second paragraph as being indefinite. Applicants have amended claim 41 to remove the term "about." In light of this amendment, Applicants respectfully request that this rejection be withdrawn.

#### **35 U.S.C. §102 Rejections**

A claim is anticipated under 35 U.S.C. §102 only if each and every element as set forth in a claim is found, either expressly or inherently described, in a single prior art reference (MPEP §2131; *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d, 628, 631, 2 USPQ2d 1051 (Fed. Cir. 1987)). A claimed invention is anticipated only when it is "known to the art in the detail of the claim." *Karsten Manufacturing Corp. v. Cleveland Golf Co.*, 242 F.3d 1376, 1383 (Fed. Cir. 2001). In other words, not only must the limitations of the claim be shown in a single prior art reference, the limitations must be "arranged as in the claim." *Id.*

The rejection of claims 33 and 36 under 35 U.S.C. §102(b) as being anticipated by Feldstein et al. (US 5,352,461) has been maintained for the reasons of record set forth on page 3 of the Office Action mailed May 17, 2006. Applicants respectfully traverse.

Claim 33 has been amended to recite that the complex is formed by the process of "a) providing pre-formed microparticles of diketopiperazine in a suspension

comprising a solvent; b) adding insulin to said suspension; and c) removing solvent from said suspension.” Feldstein does not disclose, either explicitly or inherently, forming complexes of insulin and diketopiperazine by complexing insulin to pre-formed microparticles of diketopiperazine according to the steps of amended claim 33. Therefore, claims 33 and 36 are not anticipated by Feldstein and Applicants respectfully request the withdrawal of the rejection on this basis.

The rejection of claims 33, 35, 37 and 38 under 35 U.S.C. §102(b) as being anticipated by Steiner et al. (US 5,503,852) has been maintained for the reasons of record set forth on pages 3-4 of the Office Action mailed May 17, 2006. Applicants respectfully traverse.

Claim 33 has been amended as discussed *supra*. Steiner does not disclose, either explicitly or inherently, forming complexes of insulin and diketopiperazine by complexing insulin to pre-formed microparticles of diketopiperazine according to the steps of amended claim 33. Therefore, claims 33, 35, 37 and 38 are not anticipated by Steiner and Applicants respectfully request the withdrawal of the rejection on this basis.

### **35 U.S.C. §103 Rejections**

It is well established that a *prima facie* case of obviousness requires that the Office provide evidence to support three basic criteria: there must be some suggestion or motivation in the cited art to modify a reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references must teach or suggest all the claim limitations. MPEP 2143.

The rejection of claims 33 and 35-39 under 35 U.S.C. §103(a) as being unpatentable over Milstein (US 5,976,569) has been maintained for the reasons of record set forth on pages 5-7 of the Office Action mailed on May 17, 2006. Applicants respectfully traverse.

Claim 33 has been amended as discussed *supra*. Milstein does not teach or suggest forming complexes of insulin and diketopiperazine by complexing insulin to pre-formed microparticles of diketopiperazine according to the steps of amended claim 33.

Therefore, because Milstein does not teach or suggest all the limitations of claims 33 and 35-39, the Office has not established *prima facie* obviousness of these claims over Milstein. Applicants respectfully request the withdrawal of the rejection on this basis.

The rejection of claims 40-42 under 35 U.S.C. §103(a) as being unpatentable over Milstein (US 5,976,569) further in view of Edelman, S.V. has been maintained for the reasons of record set forth on pages 7-9 of the Office Action mailed on May 17, 2006. Applicants respectfully traverse.

Claim 33, from which claims 40-42 depend, has been amended as discussed *supra*. Milstein does not teach or suggest forming complexes of insulin and diketopiperazine by complexing insulin to pre-formed microparticles of diketopiperazine according to the steps of amended claim 33, and consequently claims 40-42. Edelman does not remedy the deficiencies of Milstein.

Therefore, claims 40-42 are not obvious over Milstein in view of Edelman and Applicants respectfully request the withdrawal of the rejection on this basis.

Therefore, because Milstein and Edelman, in combination, do not teach or suggest all the limitations of claims 40-42, the Office has not established *prima facie* obviousness of these claims over Milstein in view of Edelman. Applicants respectfully request the withdrawal of the rejection on this basis.

### **Double Patenting**

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 over claims 1, 4-7 and 10-14 of US Patent No. 6,071,497 (hereinafter "the '497 patent") has been maintained for the reasons of record set forth on page 10 of the Office Action mailed May 17, 2006.

The policy behind the judicially-created doctrine of obviousness-type double patenting is "to prevent the unjustified or improper timewise extension of the 'right to exclude' granted by a patent." However, the Applicants respectfully submit that

allowance of the Applicants' pending claims 33 and 35-39 would clearly not lead to an improper timewise extension of the claims in U.S. Patent 6,071,497.

The claims of the instant application are drawn to a delivery formulation for monomeric or dimeric insulin comprising particles formed by complexing insulin to pre-formed microparticles of diketopiperazine according to a claimed process.

The claims of the '497 patent are drawn to microparticulate systems and methods for delivery comprising microparticles incorporating therapeutic, prophylactic or diagnostic agents. The microparticles of the '497 patent have the agent incorporated into the particle, rather than complexed on the surface of the particle, as do the instant claims.

Thus, the methods and systems recited in claims 1, 4-7 and 10-14 of the '497 patent do not read on the methods recited in claims 33 and 35-39 of the instant application. Additionally, there is nothing in the art that teaches or suggests that the methods covered by the Applicants' claims are equivalent to the methods and systems covered by the claims of the '497 patent, which would allow the Applicants to make a claim that someone using the methods and systems covered by the '497 patent would be infringing the Applicants' claims. Moreover, the Applicants' claims are not just obvious variations of claims 1, 4-7 and 10-14 of the '497 patent that would extend the patent term of the '497 patent. Therefore, Applicants respectfully request the withdrawal of the double patenting rejection of instant claims 33 and 35-39 over claims 1, 4-7 and 10-14 of the '497 patent.

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 over claims 1, 4-7 and 10-12 of US Patent No. 6,428,771 (hereinafter "the '771 patent") has been maintained for the reasons of record set forth on page 10-11 of the Office Action mailed May 17, 2006.

The policy behind the judicially-created doctrine of obviousness-type double patenting is "to prevent the unjustified or improper timewise extension of the 'right to exclude' granted by a patent." However, the Applicants respectfully submit that

allowance of the Applicants' pending claims 33 and 35-39 would clearly not lead to an improper timewise extension of the claims in U.S. Patent 6,428,771.

The claims of the instant application are drawn to a delivery formulation for monomeric or dimeric insulin comprising particles formed by complexing insulin to pre-formed microparticles of diketopiperazine according to a claimed process.

The claims of the '771 patent are drawn to microparticulate systems and methods for delivery comprising microparticles incorporating therapeutic, prophylactic or diagnostic agents. The microparticles of the '771 patent have the agent incorporated into the particle, rather than complexed on the surface of the particle, as do the instant claims.

Thus, the methods and systems recited in claims 1, 4-7 and 10-12 of the '771 patent do not read on the methods recited in claims 33 and 35-39 of the instant application. Additionally, there is nothing in the art that teaches or suggests that the methods covered by the Applicants' claims are equivalent to the methods and systems covered by the claims of the '771 patent, which would allow the Applicants to make a claim that someone using the methods and systems covered by the '771 patent would be infringing the Applicants' claims. Moreover, the Applicants' claims are not just obvious variations of claims 1, 4-7 and 10-12 of the '771 patent that would extend the patent term of the '771 patent. Therefore, Applicants respectfully request the withdrawal of the double patenting rejection of instant claims 33 and 35-39 over claims 1, 4-7 and 10-12 of the '771 patent.

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of (1) claims 33, 35-39 and 42 over claims 23-26 and 40-46 of copending Application No. 10/706,243; (2) claims 33-39 and 42 over claims 1-5, 8-10, 16-17, 23-24, 26-30 and 36 of copending Application No. 11/210,710; and (3) claims 33-35 and 40-42 as being unpatentable over claims 1-5 and 17-23 of copending Application No. 11/329,686 have been maintained for the reasons of record set forth on page 12-15 of the Office Action mailed May 17, 2006.

The Applicants respectfully request that the provisional nonstatutory obviousness-type double patenting rejections be held in abeyance until the Examiner issues an indication of allowability in this application.

**Conclusion**

In light of the claim amendments and arguments presented supra, Applicants respectfully assert that the pending claims are in condition for allowance and request that a timely Notice of Allowance be issued in this case.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

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